

EXHIBIT B

**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION**

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
THIS DOCUMENT RELATES TO: <i>Wave 5 Cases</i>	

EXPERT REPORT OF STEVEN GOLDWASSER, M.D.

TVT General Report of Steven Goldwasser, M.D.

This report contains my general opinions regarding the design, safety, and efficacy of the Gynecare TVT and TVT-Exact. It also contains a summary of my qualifications, training, education, and experience, which help form the basis of the opinions contained herein. The materials I have reviewed that support my opinions are either identified in this report or are set forth in my reliance list which will be provided with this report. All of the opinions in this report are held to a reasonable degree of medical certainty, and I reserve the ability to supplement or modify these opinions if additional information is received and/or reviewed.

BACKGROUND, TRAINING AND EXPERIENCE

I am board-certified in Obstetrics and Gynecology, with a subspecialty board certification in Female Pelvic Medicine and Reconstructive Surgery. I received my undergraduate education at the University of California, San Diego and my medical degree from Tulane University. I completed my residency in Obstetrics and Gynecology at the University of Tennessee, Memphis. Subsequently, I completed a 2-year fellowship in Female Pelvic Medicine and Reconstructive Surgery at Good Samaritan Hospital in Cincinnati Ohio under the direction of Mickey Karram, MD. After completing my fellowship training in 2000, I joined the faculty at the University of Florida in Jacksonville where I started the division of Urogynecology. In 2006, I started my private practice in Jacksonville and I continue my association with the university as a clinical instructor.

I became a diplomate of the American Board of Obstetrics and Gynecology in 2002 and became subspecialty certified in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) in 2013. I have had a Florida Medical License continuously for the past 16 years. My hospital

affiliations include Baptist Medical Center, St. Vincent's Medical Center, and the University of Florida Medical Center, Jacksonville.

During the course of my career, I have received extensive training in female pelvic medicine and reconstructive surgery, including vaginal, abdominal, laparoscopic, robotic, and non-surgical approaches for treating pelvic organ prolapse and urinary incontinence. I have obtained extensive experience in both the design and implementation of various techniques involving native tissue repair and augmentation procedures using both biologic and synthetic graft materials. I began my training on the surgical procedures for urinary incontinence during my residency from 1994 to 1998. During that time we were performing mainly Burch / MMK procedures and pubovaginal bladder neck slings. I continued performing those procedures as I started my Urogynecology fellowship in 1998. The slings at this point were constructed with a variety of materials including autologous or cadaver fascia as well as "mini slings" utilizing synthetic materials. These slings were placed at the bladder neck. We would typically use slings for more severe incontinence – those with intrinsic sphincter deficiency (ISD). The MMK / Burch procedure was usually used for less severe incontinence and / or a hypermobile urethra. These procedures typically resulted in at least an overnight hospital stay and most of these patients were discharged home with an indwelling Foley catheter. Additionally, a considerable number of these patients experienced some degree of postoperative voiding dysfunction and overactive bladder symptoms.

A short time into my fellowship (mid 1998) I was introduced to the retropubic TVT procedure as it was first made available in the United States. I remember Dr. Karram saying that this would revolutionize the way we treat stress urinary incontinence and that it did. TVT is a minimally invasive outpatient procedure. Unlike the prior SUI operations, TVT is an outpatient

procedure that can be performed under a local anesthetic. It is uncommon for patients to need a Foley catheter post procedure. Post-op pain is easily managed with NSAIDS or in many cases no pain medication. It has proven very effective for SUI both with and without ISD and mixed incontinence. Since my fellowship, it has been and continues to be my procedure of choice. Since I started using the TVT in 1998, hundreds of studies in the US and Europe have evaluated the procedure and echo the safety, efficacy, and long lasting durability I have personally experienced. In a 17-year follow up study on the TVT procedure, Nilsson et al found that over 90% of the women were objectively continent and 87% were subjectively cured or significantly improved. Nilsson, C.G., Palva, K., Aarnio, R. et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence, *Int Urogynecol J* (2013) 24: 1265).

Over the past 19 years, I have performed easily over 1000 TVT procedures (predominantly the original TVT and the TVT Exact) with excellent results. The vast majority of patients comment that they only wish they had done this sooner as it has been an amazing positive life change that has allowed them to get back to their normal level of physical activity. The TVT procedure is one of the most predictable and reliable surgical remedies in urogynecology. Currently, my retropubic sling of choice is the TVT Exact and I continue to perform the TVT Exact on a weekly basis. My patients continue to see excellent results. I have seen very few adverse events. In the past several years, plaintiff's attorneys have embarked on a huge self serving campaign to actively encourage patients to enter into lawsuits by advertising unsubstantiated and exaggerated claims. This has created a wave of unfounded patient fear and anxiety that I have personally seen in my practice. Subsequently, there has been a 30% reduction in the number of patients undergoing stress incontinence and pelvic reconstructive surgery.

Perkins CE, Warrior K, Eilber KS, et al. The Role of Mid-urethral Slings in 2014: Analysis of the Impact of Litigation on Practice. *Curr Bladder Dysfunct Rep.* (2015) 10:39–45; Koo K, Gormley EA. Transvaginal Mesh in the Media Following the 2011 US Food and Drug Administration Public Health Notification Update. *Neurourol. Urodynam.* 2017 Feb; 36(2):329-332.

Beginning with my career in 2000 as the Chief of Urogynecology at the University of Florida and through my transition into private practice, I continue to train residents on the TVT procedure. I also served as an instructor in conjunction with the Ethicon professional education program in training other surgeons on the TVT procedure, including Urogynecologists, Urologists, and Gynecologists from around the country. During the course of product development and as an instructor for physician training, I dedicated considerable time to cadaver lab dissection. My extensive clinical training and cadaver dissection experience led to my development and implementation of several devices and techniques for reconstructive pelvic surgery. This experience led to a collaborative effort with my urology colleague from the University of Florida. Ultimately, we developed the EXAIR, a novel polypropylene mesh graft-based approach for treating vaginal prolapse.

Given my background, training, education, and experience, attendance and participation in medical meetings, and teaching other physicians, I am familiar with, and can testify regarding, the relative risks and benefits of the various approaches for treating stress urinary incontinence, as well as the possible complications for the various approaches. In addition, a portion of my practice involves re-operative management of recurrent urinary incontinence and prolapse, as well as treating and managing complications associated with both mesh and non-mesh surgical procedures. I also have considerable experience treating complex female pelvic pain, sexual

dysfunction, complex urinary incontinence, recurrent urinary tract infections, and other pelvic complaints in patients. Therefore, I understand, and can testify about, contributing causes of different patient complaints, as well as the best ways to avoid, minimize, or treat complaints when they occur.

I am also familiar with, and can testify regarding, the development and application of polypropylene based mesh materials incorporated in treating female stress urinary incontinence and repairing vaginal prolapse, as well as the appropriate surgical applications for mesh and the associated risks and benefits. I am also aware of and can testify regarding how physicians are trained, what information is provided during their training, how physicians get information they rely on in performing surgical procedures, and the different ways physicians remain knowledgeable of the data and advances in medicine relevant to this field. A copy of my CV, which further details my training, education and experience, is attached to this report.

Since the development of the polypropylene midurethral sling by Dr. Ulmsten in the 1990's, the TVT procedure is the most studied midurethral sling with the longest track record. Because of its long-term efficacy, safety profile and simplicity, it is now the "gold standard" for the treatment of female stress urinary incontinence. Cox A, Herschorn S, Lee L., Surgical management of female SUI: Is there a gold standard? Nat Rev Urol 2013;10:78-89. A recent survey indicates that these procedures are used by 99% of the membership of the American Urogynecologic Society, the premier organization dedicated to the treatment of female pelvic floor disorders. Clemons et al., Impact of the 2011 FDA Transvaginal Mesh Safety Update on AUGS Members Use of Synthetic Mesh and Biologic Grafts in Pelvic Reconstructive Surgery. Female Pelvic Med Reconstr Surg. 2013;19:191-198.

URINARY INCONTINENCE AND QUALITY OF LIFE

Urinary incontinence is involuntary loss of bladder control. Symptoms can range from mild “leaking” drops of urine to uncontrollable wetting. Women experience urinary incontinence twice as often as men. It can occur at any age but is more common as women age. It is often a debilitating problem both physically, emotionally and may have a major impact on quality of life. A 2015 Cochrane review notes that 50% of women will experience urinary incontinence at some point in their lives and of these women, 30–80% experience SUI. Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7. The November 2015 ACOG/AUGS Practice Bulletin on Urinary Incontinence in Women states that the “estimated direct cost of urinary incontinence care in the United States is \$19.5 billion.” ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.

The three basic types of urinary incontinence are stress incontinence (SUI), urge incontinence (UII) and mixed incontinence which is a combination of SUI and UII.

UII occurs secondary to an uninhibited contraction of the detrusor muscle or a “bladder spasm.” It can be successfully treated with behavioral modification, physical therapy, medication, sacral nerve stimulation and Botox injections into the detrusor muscle.

Stress urinary incontinence is the involuntary loss of urine due to physical activity such as a cough, sneeze or exercise, etc. The focus of SUI is the urethra. The proposed mechanism of action for the development of stress urinary incontinence is loss of urethral support or dynamic compression due to weakening of the pubourethral ligaments and loss of intrinsic sphincter tone. There are many risk factors for developing stress incontinence including previous pelvic surgery, pregnancy with vaginal delivery, increasing age, obesity, diabetes, smoking, and family history.

DIAGNOSING STRESS URINARY INCONTINENCE

SUI is diagnosed by history, bladder questionnaire, physical examination, cough test, bladder diary, cystometric studies, and cystoscopy.

TREATMENT OPTIONS FOR SUI

Nonsurgical treatment options for SUI include behavior modification, timed voiding, pelvic floor physical therapy, biofeedback, incontinence pads, incontinence pessaries, and urethra bulking procedures. Depending upon the severity of symptoms and the level of bother, many women often ultimately select a surgical remedy.

Surgical management is often considered to be the most definitive long-term treatment for stress urinary incontinence. Prior to the advent of the modern midurethral synthetic sling, traditional surgical approaches over the past 100 years include the abdominal retropubic urethropexy (Burch (1961) and MMK (1949) colposuspensions), bladder neck slings (“fascial slings”), and needle urethral suspensions (Pereya (1959)), and the Kelly plication (1912)).

The traditional anti-incontinence procedures were based upon older theories of the pathophysiology behind stress urinary incontinence. These theories focused on the pressure transmission between the increased abdominal pressure (cough or sneeze) and a simultaneous reduction in urethral closure pressure, which results in stress incontinence. Alan J. Wein, Louis R. Kavoussi, Andrew C. Novick, Alan W. Partin, Craig A. Peters. Campbell-Walsh Urology, 10th Ed. Rev., Elsevier Saunders, 2012; DeLancey JO, Structural support of the urethra as it relates to stress urinary incontinence: the hammock hypothesis. Am J Obstet Gynecol. 1994 Jun;170(6):1713-20.

These surgeries have shared risks including: hematoma, bladder and bowel injury, urethral and ureteral injury, vascular injury, infection, voiding dysfunction, persistent SUI,

bleeding, pain, dyspareunia, fistula, and new onset or worsening urge incontinence. ACOG / AUGS Practice Bulletin No. 155; Nov. 2015. Additionally these procedures, relative the TVT, are more invasive, require a longer hospital stay, have longer operative times, increased voiding dysfunction and prolonged catheterization. Urethral suspension procedures performed through the abdomen (Burch, MMK, Raz) have been shown to be effective in the short term, but have lower long term cure rates. Brubaker, L., Abdominal sacrocolpopexy with Burch colposuspension to reduce urinary stress incontinence. N Engl J Med.; 354(15): 1557-1566 (2006); Albo ME, Burch colposuspension versus fascial sling to reduce urinary stress incontinence. N Engl J Med.; 356:2143-55 (2007).

EVOLUTION OF MESH

Surgical mesh was designed in the 1950s to correct abdominal wall hernias. The woven material is placed below the skin to patch the weakened area in the abdomen and block intestines and other tissues from protruding. Abdominal wall hernia repair with mesh is now standard in most countries and widely accepted as superior to primary suture repair. As a result, there has been a rapid growth in the variety of meshes available. In 1958, Usher published his technique using a polypropylene mesh. This led to the Lichtenstein repair years later, which popularized mesh for hernia repair. In 2002, the EU trial collaboration analyzed 58 randomized controlled trials and found that the use of mesh was superior to other techniques. The EU Hernia Trialists Collaboration. Repair of groin hernia with synthetic mesh: meta-analysis of Randomized Controlled Trials. Ann Surg. 2002;235(3):322–32. They observed fewer recurrences and less postoperative pain with the mesh repair. Mesh has now virtually replaced suture repair of abdominal wall hernia in the developed world.

The successful treatment of hernias with surgical mesh led doctors to consider using it in other parts of the body that required additional support. In the 1950s gynecologists first recognized the need for graft augmentation in prolapse surgery to improve the disappointing surgical outcomes from vaginal colporrhaphy. Around 1962, the abdominal sacrocolpopexy (ASC) began to be performed. Lane first described the use of graft material for sacrocolpopexy procedures (e.g., harvested fascia lata, abdominal fascia, cadaveric fascia lata, Marlex, Prolene, Gore-Tex, Mersilene) with variable success rates. Lane F.E., Repair of posthysterectomy vaginal-vault prolapse. *Obstet Gynecol* 1962 Jul; 20: 72–77. In 1970, Morgan reported the use of Marlex for stress urinary incontinence (SUI). Morgan JE, A sling operation, using Marlex polypropylene mesh, for treatment of recurrent stress incontinence. *Am J Obstet Gynecol*. 1970 Feb 1;106(3):369-77.

In 1998, the Ethicon retropubic TVT sling device was introduced in the United States (discussed below). It is composed of a Type 1 lightweight, macroporous, monofilament polypropylene mesh. The Amid classification separates materials based on pore size, which can impact infectious risk and tissue integration. In general, a pore size of $>75\text{ }\mu\text{m}$ is considered macroporous and is desirable, as it allows passage of leukocytes and macrophages. This is classified as a Type 1 Mesh. Woven meshes and meshes with smaller pore sizes ($<75\text{ }\mu\text{m}$) allow bacteria to pass into the material and evade the host's defense mechanisms (leukocytes and macrophages cannot pass into the material). Additionally, pore size of $>75\text{ }\mu\text{m}$ (Type 1 Mesh) also allows capillary and tissue growth into the mesh pores, which prevents encapsulation and promotes support to the prolapsed organ(s). The pore size of TVT is approximately 1.3 mm or 1,379 μm , which easily accommodates the cells and small blood vessels needed to access the pores, promotes tissue integration, and reduces the risk of

infection. Type 1 mesh remains the preferred material for surgical treatment of SUI. It has numerous advantages over other graft materials including a low failure rate in incontinence and prolapse surgery.

As noted above, the mesh in the TVT and TVT-Exact devices is lightweight mesh, not “heavyweight” mesh. Synthetic slings require certain characteristics to properly support the urethra in order to avoid adversely affecting its function. The Nilsson seventeen-year follow-up data substantiates the biocompatibility of the weight/stiffness/elasticity and porosity of the TVT mesh. See also 2014 AUGS/SUFU position statement. There is also no strong scientific evidence that a lighter weight mesh like Ultrapro or Vypro, or other meshes used for hernia repair, would work as well in the design of the TVT or TVT-Exact. These meshes have not been shown in studies or medical literature to be safer or more efficacious in the treatment of stress urinary incontinence. They also lack long term data for treating stress incontinence as is available for the TVT mesh. See literature cited in this report. In fact, those products are not available in the United States for use as a sling. Further, I have seen documents noting that when sampled, a majority of pelvic surgeons (65%) advised that they rejected the use of the partly absorbable meshes in the sling application due to various reasons (including a lack of need given the clinical data on the TVT, concerns with a lack of long term efficacy, and the fact that there could still be exposures and other complications). [ETH.MESH.02219584].

Some have suggested that use of biologic grafts made of cadaveric or xenograft (animal) material would be safer and more effective than polypropylene mesh. However, this has never been demonstrated in the literature or data. Biologic grafts were abandoned by most physicians in the 1990s to the early 2000s due to high complication rates, integration concerns, disease transmission (hepatitis, HIV, etc.), low efficacy/durability, and concerns costs and

supply. Handa et al., Banked human fascia lata for the suburethral sling procedure: a preliminary report. *Obstet Gynecol.* 1996 Dec;88(6):1045-9; Woodruff et al., Histologic comparison of pubovaginal sling graft materials: a comparative study. *Urology.* 2008 Jul;72(1):85-9; Krambeck et al, Time-dependent variations in inflammation and scar formation of six different pubovaginal sling materials in the rabbit model. *Urology.* 2006 May;67(5):1105-10; Fitzgerald et al, Failure of allograft suburethral slings. *BJU Int.* 1999 Nov;84(7):785-8. The data on biologic grafts do not demonstrate that it is a safer or more effective alternative to the TVT. Trends in the use of the midurethral sling show that it is the preferred method to treat stress urinary incontinence by an overwhelming margin.

With respect to autologous slings, harvesting fascia from the abdomen or thigh carries unique risks of pain, nerve entrapment, and infection, which is why it is not considered by many to be a good option as compared to polypropylene slings. The ACOG and AUGS recommend that autologous fascial bladder neck slings be considered for women who decline or are not candidates for synthetic mesh slings. ACOG / AUGS Practice Bulletin No. 155; Nov. 2015. The AUA 2012 Update to the SUI Guidelines reported higher rates of pain and sexual dysfunction with pubovaginal slings than with midurethral slings. Guideline for the Surgical Management of Female Stress Urinary Incontinence: 2009 Update Appendices A11 and A16. The Albo trial (SISTER) cited above is the largest multicenter RCT that compares autologous slings to the Burch colposuspension. In that study, 655 women were followed for two years. Success as defined by the study was reported as 66% for the pubovaginal sling group versus 49% in the Burch group. Voiding dysfunction was reported in 14% of women in the pubovaginal sling group with 6% needing surgical revision for persistent voiding dysfunction. Average blood loss was 229ml and 238 ml, and average operating time was 136 and 138

minutes. Serious adverse events were reported in 13% in the pubovaginal sling group and 10% of the Burch group. Wound complications occurred in 25% of the total cases and 4% of those complications requiring surgical intervention. See also Brubaker L. 5-Year Continence Rates, Satisfaction and Adverse Events of Burch Urethropexy and Fascial Sling Surgery for Urinary Incontinence. *Urology*. 2012;187:1324–1330; Richter et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. *Urology*. 2012;188:485–489.

DEVELOPMENT OF TVT

The retropubic TVT was the first mid-urethral sling developed for treating stress urinary incontinence. Dr. Ulmsten in Sweden developed the TVT in the early 1990's. The procedure involves the tension free placement of a Prolene mesh sling at the level of the midurethra. The sling functions by dynamically compressing the midurethra during episodes of physical activity (increased bladder pressure) subsequently reducing or stopping SUI. The indications for a mid urethral sling include urethral hypermobility, intrinsic sphincter deficiency, mixed incontinence with a predominance of stress incontinence symptoms and recurrent stress urinary incontinence. There are two ways to place a midurethral sling – the procedure can be performed with a retropubic approach or a transobturator approach. The focus of this report is on the retropubic TVT and TVT Exact sling. The primary difference between the TVT and the Exact is the introducer. The TVT has a reusable stainless steel introducer and the Exact has a plastic single use introducer.

TVT is single use device, consisting of one piece of undyed or blue Prolene polypropylene mesh (tape) approximately 1/2 x 18 inches (1.1 x 45 cm) which is covered by a plastic sheath cut and overlapping in the middle, and held between two stainless steel needles

bonded to the mesh and sheath with plastic collars. The TVT device is available in either mechanical cut or laser cut versions for the physician's preference. To determine if the TVT device implant is mechanical or laser cut, consult the product code on the device packaging; an (L) at the end of the number indicates the laser cut mesh.

Prolene mesh is constructed of knitted filaments of extruded polypropylene strands identical in composition to that used in Prolene polypropylene nonabsorbable surgical suture. The mesh is approximately 0.027 inches (0.7 mm) thick. This material, when used as a suture, has been reported to be non-reactive and to retain its strength indefinitely in clinical use.

The retropubic midurethral tension free synthetic sling is based on the "Integral Theory" of Ulmsten and Petros. Ulmsten, U., Petros, P., Intravaginal slingplasty (IVS): an ambulatory surgical procedure for treatment of female urinary incontinence. *Scand. J. Urol. Nephrol.* 29: 75–82, (1995). They postulated that the pubourethral ligament, the suburethral hammock of the anterior vaginal wall and the pubococcygeus muscles are closely integrated and coordinated to affect the separate opening and closure of the urethra and bladder neck. A defect in these structures or their interaction will result in urinary incontinence or voiding dysfunction. This theory is a rethinking of the continence mechanism upon which the traditional incontinence procedures were based. The Integral theory on the pathophysiology of stress urinary incontinence demonstrated the importance of mid-urethral support provided by the pubourethral ligaments, and the elasticity of the anterior vaginal wall that effectively transmits the contractions of the pubococcygeous and levator ani muscles to affect the separate closure of the urethra and bladder neck. Dr. Ulmsten and colleagues incorporated the Integral Theory into the design of the retropubic TVT. The TVT effectively replaces the dysfunctional pubourethral ligament and the suburethral vaginal support in a tension free minimally invasive way that more

closely approximates normal anatomy. The advent of the TVT procedure is a leap forward in the treatment of SUI. The critical modification of positioning the sling at the midurethra (rather than at the bladder neck) has reduced the complication of voiding dysfunction and urinary retention. The TVT has been used extensively in Europe for the treatment of SUI and was introduced to the U.S. in 1998, leading the way for the mid-urethral sling to become the gold standard for SUI surgery. Cox A, Herschorn S, Lee L., Surgical management of female SUI: Is there a gold standard? Nat Rev Urol 2013;10:78-89. The mid-urethral sling has become the therapy of choice for the treatment of SUI with several million procedures performed worldwide. The TVT has a demonstrated long-term durability, safety and efficacy up to 17 years. 2014 AUGS/SUFU position statement.

During the development process, early prototypes for the TVT device critically evaluated the use of a variety of these synthetic materials, such as Mersilene and Gortex which were found to have higher exposure rates. Petros P, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond. 2015 Apr;26(4):471-6; Ulmsten et al, An ambulatory surgical procedure under local anesthesia for treatment of female incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 1996;7(2):81-5. These synthetic materials (Gore-Tex, Teflon, Mersilene) were found to be associated with a significant inflammatory reaction in paraurethral tissues and caused a significant amount of tape rejection. Falconer C, et al, Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. Int Urogynecol J., (2001) 12(Suppl 2): S19.

DEVELOPMENT OF TVT-EXACT

The TVT-Exact was launched in 2010 and is a retropubic midurethral sling made of laser-cut Prolene polypropylene mesh. It is 1.1 cm x 45 cm. The mesh used in the TVT-Exact

is covered by a clear plastic implant sheath and held between two trocar sheaths that are bonded to the TVT-Exact implant and implant Sheath. The mesh used in the TVT-Exact is the same lightweight, macroporous, monofilament mesh that is used in the TVT device. The trocars of the TVT-Exact are longer and slightly thinner (3 mm v. 5 mm) than the TVT trocars. A study of almost a hundred patients receiving either TVT or TVT-Exact who were followed for at least a year found no significant difference in the rate of bladder injury. Thubert T, et al. Bladder injury and success rates following retropubic mid-urethral sling: TVT EXACT vs. TVT. Eur J Obstet Gynecol Reprod Biol. 2016 Mar;198:78–83. The study found less intense immediate post-operative pain in the TVT-Exact cohort, but by six weeks after surgery the prevalence of pain no longer differed between the two groups. There was an increased PVR in the TVT-Exact group, but there was no in post-operative self-catheterization. The rate of tape release or cutting was also comparable in the two groups. The prevalence of perioperative and post-operative complications was equal in the two groups, and there was no significant difference in the success rate (no reported SUI and negative cough stress test). In my clinical experience I have had excellent patient outcomes with both versions of the TVT but I do prefer the handling and the thinner trocars of the TVT Exact which is why it is currently the sling I use. Other colleagues continue to use the TVT with excellent results.

DATA SUPPORTING SAFETY AND EFFECTIVENESS OF TVT / TVT-EXACT

In preparing this report and throughout my career, I have done an extensive review of the literature evaluating the surgical management of stress urinary incontinence. Midurethral synthetic slings, and the TVT in particular, have been extensively studied. It is the most extensively studied incontinence procedure to date. Randomized controlled trials have demonstrated that the synthetic midurethral slings are equally if not more effective than

traditional surgeries (Burch colposuspension and pubovaginal slings). The midurethral slings are also associated with less morbidity and cost. Additionally, they require significantly less time to perform and are much easier to teach. They have also been shown to improve quality of life as well as, if not better than, the traditional SUI operations.

The 2015 Cochrane review included 81 trials that had a total of 12,113 women comparing the transobturator route and the retropubic route. The authors concluded that the midurethral sling is a safe and effective procedure that improves quality of life with minimal risk of adverse events. This review provides:

Main findings of this review

We performed a thorough search of the medical literature up to June 2014. We identified 81 trials that had a total of 12,113 women. These trials showed that over 80% of women with stress urinary incontinence are cured, or have significant improvement in their symptoms, with either operation, for up to five years after surgery. We found this to be the case irrespective of the tapes used and the route of tape insertion. The studies used different questionnaires to assess quality of life, which meant that we could not combine their results for analysis. However, the information that is available for quality of life shows that it improves as a result of these operations, though there is no clear difference between the two procedures. Only a few trials provided information about the effectiveness of these tapes more than five years after surgery. The evidence that we have been able to assess indicates that the positive effects persist.

Adverse effects

Tapes passing behind the pubic bone (retropubic) seem to carry a greater risk of injuring the bladder during the operation and of women experiencing problems emptying their bladder completely after surgery. However, this operation leads to less groin pain in the short term. There is some limited evidence that this way of inserting the tape has a lower risk of requiring a repeat operation in the long term compared to tapes passing through the groin (transobturator). There is moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes.

Authors' conclusions

Mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI. With the exception of groin pain, fewer adverse events occur with employment of a transobturator approach. When comparing transobturator techniques of a medial-to-lateral versus a lateral-to-medial insertion, there is no evidence to support the use of one approach over the other. However, a bottom-to-top route was more effective than top-to-bottom route for retropubic tapes.

Schimpf et al (Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;210:1.e1-1.e27) conducted an extensive review of the MEDLINE and Cochrane Central Register for Controlled Trials from Jan. 1, 1990 through April 12, 2013. Their results are as follows:

For midurethral slings (MUS) vs Burch, metaanalysis of objective cure showed no significant difference (OR, 1.18; 95% confidence interval [CI], 0.73e1.89). Therefore, we suggest either intervention; the decision should balance potential adverse events (AEs) and concomitant surgeries. For women considering pubovaginal sling vs Burch, the evidence favored slings for both subjective and objective cure. We recommend pubovaginal sling to maximize cure outcomes. For pubovaginal slings vs MUS, metaanalysis of subjective cure favored MUS (OR, 0.40; 95% CI, 0.18e0.85). Therefore, we recommend MUS. For obturator slings vs retropubic MUS, metaanalyses for both objective (OR, 1.16; 95% CI, 0.93e1.45) and subjective cure (OR, 1.17; 95% CI, 0.91e1.51) favored retropubic slings but were not significant. Metaanalysis of satisfaction outcomes favored obturator slings but was not significant (OR, 0.77; 95% CI, 0.52e1.13). AEs were variable between slings; metaanalysis showed overactive bladder symptoms were more common following retropubic slings (OR, 1.413; 95% CI, 1.01e1.98, P 1/4 .046). We recommend either retropubic or obturator slings for cure outcomes; the decision should balance AEs. For minislings vs full-length MUS, metaanalyses of objective (OR, 4.16; 95% CI, 2.15e8.05) and subjective (OR, 2.65; 95% CI, 1.36e5.17) cure both significantly favored full-length slings. Therefore, we recommend a full-length MUS.

Cox et al (Surgical management of female SUI: is there a gold standard? *Nat Rev Urol* 2013;10:78-89) concluded that "Randomized controlled trials have demonstrated that synthetic

midurethral slings are just as effective as traditional procedures (such as Burch colposuspension and pubovaginal slings) but with less associated morbidity.” The table below was also provided:

Table 1 Meta-analyses of midurethral slings versus traditional procedures for stress urinary incontinence			
Study	Comparison	Subjective success at 12 months	Objective success at 12 months
Rehman <i>et al.</i> (2011) ¹	Pubovaginal fascial sling vs midurethral sling	Equal success (<i>n</i> =693) RR 0.97 (95% CI 0.78–1.20)	Equal success* (<i>n</i> =160) RR 1.29 (95% CI 0.45–3.71)
Novara <i>et al.</i> (2010) ²	Midurethral sling vs Burch colposuspension	Equal success (<i>n</i> =400) OR 0.79 (95% CI 0.52–1.21; <i>P</i> =0.27)	Favored midurethral sling (<i>n</i> =528) OR 0.38 (95% CI 0.25–0.57; <i>P</i> =0.0001)
Novara <i>et al.</i> (2010)	Midurethral sling vs pubovaginal sling	Equal success (<i>n</i> =281) OR 1.28 (95% CI 0.74–2.23; <i>P</i> =0.38)	Equal success (<i>n</i> =473) OR 0.8 (95% CI 0.51–1.26; <i>P</i> =0.35)
Ogah <i>et al.</i> (2009) ³	Midurethral sling vs pubovaginal sling	Equal success (<i>n</i> =599) RR 1.03 (95% CI	NR

¹ Rehman, H., Bezerra, C. C., Bruschini, H. & Cody, J. D., Traditional suburethral sling operations for urinary incontinence in women. Cochrane Database Syst. Rev. CD001754 (2011).

² Novara, G. et al., Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. Eur. Urol. 58, 218–238 (2010).

		0.94–1.13)	
Ogah <i>et al.</i> (2009)	Midurethral sling vs open Burch colposuspension	Equal success (<i>n</i> =729) RR 0.96 (95% CI 0.90–1.03)	Equal success (<i>n</i> =468) RR 1.04 (95% CI 0.94– 1.14)
*At >12 months. Abbreviation: NR, not reported.			

Table 2 | Meta-analyses of midurethral slings versus laparoscopic Burch procedure

Study	Comparison	Follow-up (months)	Subjective success	Objective success
Ogah <i>et al.</i> (2009)	Midurethral sling vs laparoscopic Burch colposuspension	12	Equal success (<i>n</i> =434) RR 1.11 (95% CI 0.99–1.24)	Favored midurethral sling (<i>n</i> =513) RR 1.15 (95% CI 1.06–1.24)
Dean <i>et al.</i> (2006) ⁴	Laparoscopic colposuspension vs midurethral sling	18	Equal success (<i>n</i> =327) RR 1.12 (95% CI 0.98–1.29)	Favored midurethral sling (<i>n</i> =534) RR 1.16 (95% CI 1.07–1.25)

ACOG and AUGS conducted a systematic review of the medical literature and issued a Practice Bulletin making recommendations for the treatment of urinary incontinence in women.

³ Ogah, J., Cody, J. D. & Rogerson, L. *Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women*. Cochrane Database Syst. Rev. CD006375 (2009).

⁴ Dean, N., Herbison, P., Ellis, G. Wilson, D. Laparoscopic colposuspension and tension-free vaginal tape: a systematic review. BJOG 2006 Dec; 113(12): 1345–1353.

ACOG / AUGS Practice Bulletin No. 155; Nov. 2015. The following recommendations were based on good and consistent (Level A) evidence:

- Initial midurethral sling surgery results in higher 1-year subjective and objective cure rates than pelvic floor physical therapy in women with stress urinary incontinence.
- Synthetic midurethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension. Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic midurethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic midurethral slings.
- There are substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress urinary incontinence in women.

Virtually all of the professional organizations and the FDA have issued guidelines and position statements affirming the safety, efficacy and widespread worldwide acceptance of synthetic mesh midurethral slings like the TVT and the TVT Exact. Some of these include:

- **AUGS-SUFU, Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 3, 2014) (updated June 2016 and supported by the American Association of Gynecological Laparoscopists, the American College of Obstetricians and Gynecologists, the National Association for Continence, the Society of Gynecologic Surgeons, and the Women's Health Foundation)**

- “Polypropylene material is safe and effective as a surgical implant. Polypropylene has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades, in millions of patients in the US and the world (personal communication with manufacturers of polypropylene suture and mesh).”

- “As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years.”
- “The monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history. A broad evidence base including high quality scientific papers in medical journals in the US and the world supports the use of the MUS as a treatment for SUI. There are greater than 2000 publications in the scientific literature describing the MUS in the treatment of SUI. These studies include the highest level of scientific evidence in the peer reviewed scientific literature. . . . No other surgical treatment for SUI before or since has been subject to such extensive investigation.”
- “Polypropylene mesh midurethral slings are a standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients. Since the publication of numerous level one randomized comparative trials, the MUS has become the most common surgical procedure for the treatment of SUI in the US and the developed world. This procedure has essentially replaced open and transvaginal suspension surgeries for uncomplicated SUI. . . . Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard for stress incontinence surgery. Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members.”

- “The polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy it has created an environment for a much larger number of women to have access to treatment. In the past, concerns over failure and invasiveness of surgery caused a substantial percent of incontinent women to live without treatment. One of the unintended consequences of this polypropylene mesh controversy has been to keep women from receiving any treatment for SUI. This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.”
- **AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders (March 2013)**
 - “The American Urogynecologic Society strongly opposes any restrictions by state or local medical organizations, healthcare systems, or insurance companies which ban currently available surgical options performed by qualified and credentialed surgeons on appropriately informed patients with pelvic floor disorders.”
 - “In a recent study involving 53 expert urologists and urogynecologists (of whom > 90% were fellowship trained) and who could select among many surgical options, the full-length synthetic midurethral sling was the preferred option in 93% for the surgical treatment of primary stress incontinence. Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard of care for stress incontinence surgery.”

- **AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence (Nov. 2011) (Revised Oct. 2013)**
 - “Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low.”
 - “Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5–10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of follow-up. Based on these data, the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques.”
- **ICS Fact Sheets: A Background to Urinary and Fecal Incontinence (July 2013)**
 - “Worldwide, midurethral slings comprised of synthetic mesh have become the treatment of choice for SUI. Long-term data are robust and demonstrate durable efficacy with a very low complication rate, particularly in experienced hands. Various techniques for sling placement and different meshes are employed according to physician preference, but all appear to be equally effective.”

- **Lucas MG, Ruud JLB, Burkhard FC, et al. EAU Guidelines on Surgical Treatment of Urinary Incontinence. Eur Urol. 2012 Dec;62(6):1118–1129.**
 - “There has been a rapid adoption of midurethral synthetic sling insertion as the first-line surgical option for SUI because it is effective, it is less invasive, and patients recover more quickly.”
 - Notes that a systematic review of midurethral slings with both open colposuspension and laparoscopic colposuspension showed that retropubic insertion of a synthetic midurethral sling gave equivalent patient-reported and superior clinician-reported cure of SUI compared with colposuspension at 12 months; transobturator insertion gave equivalent patient-reported and clinician-reported cure of SUI at 12 months. Also notes that midurethral sling insertion was associated with a lower rate of new symptoms of urgency and voiding dysfunction compared with colposuspension.
- **NICE clinical guideline 171. Urinary incontinence: The management of urinary incontinence in women. (Sept. 2013)**
 - Notes that if conservative management for SUI has failed, the surgeon should offer, among other options, a synthetic midurethral tape.
 - Notes that, when offering a synthetic midurethral tape procedure, surgeons should use procedures and devices for which there is current high quality evidence of efficacy and safety. Footnote 11 then notes that at the time of publication, TVT and TVT-O (among others) met this guideline.
- **FDA, Considerations about Surgical Mesh for SUI (March 2013)**
 - “Mesh sling procedures are currently the most common type of surgery performed to correct SUI. Based on industry estimates, there were approximately 250,000 of these procedures performed in 2010.”

- “The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year. Longer follow-up data is available in the literature, but there are fewer of these long-term studies compared to studies with one-year follow-up.”
- **FDA Executive Summary, Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence (Sept. 8–9, 2011)**
 - Notes that the Burch has a long history, but its popularity has declined over the past two decades with the introduction of less invasive procedures. Notes that pubovaginal sling procedures using biologic graft material (often autologous fascia) similarly have declined in popularity.
 - Notes that anterior repair with Kelly plication to correct SUI in the presence of a cystocele and bladder neck needle suspension is rarely performed currently due to poor long-term outcomes.
 - “A substantial number of quality clinical trials, as well as systematic reviews, have been published for the first generation minimally invasive slings that provide evidence of safety and effectiveness of these devices.”
 - “After considering all available data on both safety and effectiveness, and considering the risk/benefit profile, it appears that new premarket clinical trials are not warranted for minimally invasive slings for SUI unless the device has new features (*e.g.* new polymer or coating) that could affect device performance.”

KNOWN RISKS AND ALLEGED DESIGN FLAWS

Plaintiffs’ experts’ claim that Prolene material used in the TVT and TVT-Exact is unsafe and defective. They make several claims including that the base polypropylene (Prolene) material is cytotoxic and that its incorporation into a mesh sling is not biocompatible. Their

claims include that the slings degrade, cause malignant transformations, infection and erosion and therefore the product is unsafe.

Contrary to these claims, polypropylene material has been considered safe and effective as a surgical implant for over five decades. It continues to be used in most surgical specialties including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology and urology. Prolene (polypropylene) is used widely as a permanent and durable surgical suture. When produced as a woven material, Prolene mesh is the consensus graft material in a number of areas in the human body. Specifically, type 1 mesh is universally recognized as possessing the highest biocompatibility with the least propensity for infection. Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7. Despite its advantages, there are well-known complications, which must also be considered (discussed below). Virtually all of the complications associated with mesh repairs are also known to occur with non-mesh repairs as well.

Dyspareunia, pelvic pain, and mesh erosion are very uncommon with the TVT and TVT Exact. See 2012 AUA update to the SUI Guidelines (pain and sexual dysfunction were higher with the Burch and autologous sling than the midurethral sling); Schimpf (2014) (dyspareunia was rare with the retropubic (<0.001%)). Overall the data show that the rates of mesh exposure with TVT are around 1 - 2.5% and are manageable. Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7 (Retropubic 2.1% (21/1000)); Schimpf et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27 (Retropubic 1.4%); Novara G et al., Complication rates of tension-free

midurethral slings in the treatment of female stress urinary incontinence: A systematic review and meta-analysis of randomized controlled trials comparing tension-free midurethral tapes to other surgical procedures and different devices. *Eur. Urol* 2008 Feb;53(2):288-308(Table 6 metaanalysis of 34 studies with >24 months follow up: TVT 1.1%.) In my practice, I have not seen a single case of contraction, and I am not aware of any literature that describes contraction associated with TVT or TVT Exact. The sheath that covers the mesh on the TVT, and TVT-Exact devices protects the tissue against trauma and helps the mesh pass through the tissue smoothly. Additionally, the protective sheath carries the forces of implantation so that the mesh retains its shape. Scar tissue that forms after any pelvic surgery contracts, and tissue incorporating into implanted mesh is no exception, but the mesh itself does not contract. Nilsson, C.G., Palva, K., Aarnio, R. et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence, *Int Urogynecol J* (2013) 24: 1265); Lukacz ES, et al. The effects of the tension-free vaginal tape on proximal urethral position: a prospective, longitudinal evaluation. *Int Urogynecol J Pelvic Floor Dysfunct.*, 2004 Jan–Feb;15(1):32–38.

My patients go home the same day as the procedure. It is a rare exception that my patients need a catheter post procedure. I let my patients resume normal activity the day after surgery – I only advise nothing per vagina and no excessive straining or heavy lifting for 3 weeks. Patient satisfaction has been assessed across numerous parameters and TVT demonstrates a high level of satisfaction in patients with respect to urine leakage, urgency to urinate, frequency of urination, capability of physical activity, social activity, ability to engage in sexual activity, and from an emotional standpoint. Wai CY, et al. Patient Satisfaction After Midurethral Sling Surgery for Stress Urinary Incontinence. *Obstet Gynecol* 2013;121:1009–16.

The Nilsson results have been substantiated by numerous other studies, including Tamussino which reviewed the Austrian registry of 7000 TVT operations and found that there were no cases of mesh rejection or intolerance reported. Nilsson, C.G., Palva, K., Aarnio, R. et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence, *Int Urogynecol J* (2013) 24: 1265).

MECHANICAL CUT AND LASER CUT

The Plaintiffs' experts claim that Prolene particles that fall off mechanically cut mesh can result in complaints of pain and mesh erosion. This is complete speculation without any scientific support. The material in any particles would be the same Prolene polypropylene material used in the mesh that as discussed above is a well-tolerated, biocompatible material.

I have reviewed reports from the plaintiffs' experts that imply that Ethicon's action to introduce laser cut mesh was in response to a clinical problem and ultimately resulted in an attempt to deceive physicians. However, prior to modifying the production process Ethicon subjected the new laser cut mesh to rigorous testing and found that the mechanical properties did not result in any clinically significant differences. They were ultimately able to establish that changing the production process did not change the essential characteristics of the laser cut mesh. In my practice I have not noted any difference in clinical results between the laser cut mesh and the mechanical cut mesh. I have no preference between the two. The clinical studies on TVT which consistently demonstrate its efficacy, durability and safety have not been shown to have a difference in results pre and post 2007 when laser cut mesh became available.

INFLAMMATION, INFECTION AND DEGRADATION

All foreign materials, including sutures, allografts, xenografts and autografts cause some degree of host immune response that can result in varying degrees of tissue inflammation.

Polypropylene causes less inflammation than other mesh and suture materials. As per the extensive general surgery literature on hernia management and later the pelvic organ prolapse experience (as previously discussed), polypropylene is now standard of care for mesh augmented vaginal hernia repair, abdominal hernia repair and the treatment of stress urinary incontinence. The studies cited above further demonstrate that there is no clinical basis for a claim that polypropylene causes an excessive inflammatory reaction which results in a high percentage of negative clinical outcomes.

In addition, numerous meta-analyses and systematic reviews show that infection of the mesh is exceedingly rare. For example, Dyrkom, et al. reported an infection rate of 0.7%. Dyrkom O, et al. TVT compared with TVT-O and TOT: results from the Norwegian National Incontinence Registry. *Int. Urogynecol J.* 2010; 21:1321-1326. I have personally implanted mesh for more than 15 years and I have only observed mesh infection on one instance that I am aware of, which involved a transobturator sling implanted by another physician. Similarly, any allegations that there are design flaws in polypropylene mesh because it allows bacteria to adhere to the mesh during implantation causing clinical infection are not supported by the substantial amount of medical literature which demonstrates the safety and efficacy of polypropylene mesh used for both prolapse repairs and to treat stress urinary incontinence.

Polypropylene in the form of suture and mesh has been used for decades. The data and literature for both mesh slings and transvaginal mesh demonstrates that polypropylene mesh remains effective over time, which supports that clinically significant degradation of the mesh does not occur. I am aware of literature that suggests that polypropylene degrades in the human body, and other literature suggests that it does not degrade. However, my clinical experience and analysis of the body of data, including the studies cited in my report, supports my opinion that

Ethicon's polypropylene mesh does not degrade in vivo, or if it does, that such degradation does not have any clinically significant effect. It is also notable that the sub-specialty societies AUGS and SUFU have also specifically addressed whether polypropylene mesh degrades over time and whether any such degradation leads to adverse clinical outcomes. AUGS-SUFU dismissed these concerns pointing to extensive peer-reviewed literature related to polypropylene mesh:

Polypropylene is a stable and well-accepted biomaterial with a history of over five decades of use in mesh implants. In recent years, concerns regarding implanted polypropylene degradation have been raised as a result of very high-magnification images that show portions of some explanted synthetic meshes with "cracked" surfaces. These surface changes were further hypothesized to lead to adverse clinical outcomes, though this is not supported by the extensive peer-reviewed literature related to polypropylene mesh repairs. Prospective studies have followed patients with implanted mid-urethral slings for 17 years and show excellent durability and safety of the procedure.

AUGS-SUFU FAQs by Providers on Mid-urethral Slings for SUI. (March 2014). As noted in the above-referenced AUGS-SUFU statement, concerns regarding degradation are based largely on reports that have detected "cracked surfaces" along portions of explanted synthetic mesh using very high scanning electron microscope magnification. These reports have hypothesized that the microscopic observations could result in adverse clinical outcomes, but that theory is inconsistent with the extensive peer-reviewed literature related to polypropylene mesh repair.

CYTOTOXICITY AND CANCER

I am not aware of any evidence that polypropylene, when used as designed for its intended purpose as a mesh implant or as a suture material, has any clinically significant cytotoxic or cancer-causing effect. Polypropylene was developed in the 1950s. Aside from other daily forms of human contact, it has been used in countless millions of surgical procedures over the past 60 years. Common sense would dictate that based on the amount polypropylene

material used in a surgical setting since its development in the 1950s, if there was a clinically significant problem, it would be a worldwide catastrophe at this point.

Moalli, et al. addressed this issue. Moalli, P, et al., Polypropylene mesh: evidence for lack of carcinogenicity. *Int Urogynecol J*. 2014 May; 25(5): 573–576. They concluded that polypropylene, which has been used extensively in humans for over five decades, is not associated with carcinogenesis. AUGS-SUFU also addressed this issue. “There is no compelling evidence supporting human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material span well over a half century world-wide.” AUGS-SUFU FAQs by Providers on Mid-urethral Slings for SUI. (March 2014). Type 1 macroporous, monofilament polypropylene has been found to be the most biocompatible biomaterial for use in the pelvic floor. Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2015 Jul 1;7.

Further data from research on midurethral polypropylene slings also indicates lack of cancer risk. King et al., 2014 reported on 2,361 patients who underwent synthetic sling placement, and found one case each of bladder and vaginal cancer for an incidence of 0.08%, with mean follow-up of 42 months. King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? *Urology*. 2014 Oct;84(4):789-92; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. *Curr Urol Rep*. 2014 Nov;15(11):453. Linder discovered only two cases amongst 2,474 who underwent polypropylene mid-urethral sling placement (0.08%) with a mean follow-up of 61.5 months. Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. *Int Urogynecol J* 2016

Sep;27(9):1333-6. Linder further found that no local cancers were detected among the 302 patients (12% of the cohort) with more than 10 years' follow-up. There is no reliable data demonstrating an association between mesh placement with subsequent cancer formation.

COMMUNICATION OF RISK INFORMATION AND PROFESSIONAL EDUCATION

It is my opinion based on my knowledge and experience as a female pelvic reconstruction surgeon, as well as the medical literature, my training of other doctors, and my attendance at professional meetings, that TVT/TVT-Exact IFUs and professional education materials adequately described the risks specific to the devices. It is notable that the IFUs specifically state that the device should be used only by physicians trained in the surgical treatment of stress urinary incontinence and specifically in the TVT device. They also noted that the IFU is not a comprehensive reference to the surgical technique for correcting Stress Urinary Incontinence. This is significant because the IFU is written for surgeons who learn how to perform any surgery in residency, fellowship, and through proctorship. It is expected that these surgeons would be experienced and knowledgeable regarding these procedures as part of meeting their standard of care. ABOG and ABU Guidelines for Learning in Female Pelvic Medicine & Reconstructive Surgery; AUGS Resident Learning Objectives. Pelvic floor surgeons do not learn how to perform surgical procedures or the risks associated with performing surgical procedures by reading an IFU. Rather, we learn these things from training, dialogue with colleagues, attendance at professional meetings, and through review of published medical literature. Surgeons are responsible for understanding the inherent risks of the surgical procedures they perform, and surgeons are also responsible for continuing to reviewing medical literature to stay up-to-date on data related to the procedures they perform.

As I have already noted above, all pelvic floor surgical procedures have certain commonly known risks. And the risks associated with the TVT and TVT-Exact procedures are almost all common to any pelvic floor surgery regardless whether mesh is utilized. These risks have been discussed in medical literature discussing pelvic floor surgeries for decades. It is commonly known that any surgery for stress urinary incontinence can potentially cause complications such as pelvic pain, nerve/vessel injury, scarring, wound complications, bleeding, damage to surrounding organs, voiding problems/retention, dyspareunia, de novo or worsened incontinence, and the need for re-operation due to complications. Surgeons also commonly know that these complications can be mild, moderate, or severe, and temporary or long-term.

The TVT and TVT-Exact IFUs warned of several risks including possible puncture or lacerations of vessels or nerves, possible injury to organs, extrusion, erosion, fistula formation, inflammation, and retention/obstruction. All pelvic floor surgeons know based on their training and basic knowledge surgery and its inherent complications that these complications may cause sequela such as pain and dyspareunia, or the need to re-operate.

While I am not a regulatory expert, I have reviewed and considered 21 C.F.R. 801.109(c), which states that risk information for devices used by licensed professionals may be omitted from product labeling if “the article is a device for which directions, hazards, warnings, and other information are commonly known to practitioners licensed by law to use the device.” This regulation further supports my opinions because identifying not only complications, but also implications of each complication, is not necessary for pelvic floor surgeons and would require a medical treatise to accompany every product.

With respect to physician training and professional education, the manufacturer is not responsible for training surgeons how to perform surgeries, but it is my opinion that it is a very

good idea for Ethicon to offer professional education courses where surgeons are exposed to experts in this area of medicine. Having taught courses for Ethicon involving the TVT, I know that each course involved a thorough discussion of the data regarding the safety and efficacy of the product. Participants were provided not only the IFU, but also training videos and other written materials. The training that Ethicon offers is intended to supplement the surgeon's training from residency, fellowship and proctorships, and it should not be viewed as a surgeon's primary source of surgical expertise. Each individual surgeon must determine whether he/she has the surgical skill, training, and knowledge to offer a particular product/procedure to their patients. I have participated in trainings offered by numerous other manufacturers and it is my opinion that the trainings and materials offered by Ethicon are tremendous.

FEES

I am currently being paid \$500.00 per hour for my time to review medical records and draft written reports; \$600.00 per hour for in-town depositions (\$6,000.00 per day for out-of-town depositions); and \$5,000.00 per day for in-town trial testimony (\$6,000 per day for out-of-town trial testimony). In the last 4 years, I have testified as a retained expert witness in a Prolift general deposition in the Ethicon pelvic mesh litigation.

The opinions set forth in my report are based on the information that is currently available to me.

I reserve the right to modify or amend these opinions if new information becomes available.

A handwritten signature in black ink, appearing to read 'St. Goldwasser', with a long horizontal flourish extending to the right.

Steven Goldwasser, M.D.